Urine Sediment Photomicrographs/Photographs

Case History CMP-04
This urine sample is from a 56-year-old male with kidney and liver failure. Laboratory data include: Specific gravity 1.012, pH = 5, blood, protein, and leukocyte esterase = positive; glucose, ketones, nitrite = negative. Crystals were soluble in HCl.

<table>
<thead>
<tr>
<th>Identification</th>
<th>Referees No.</th>
<th>Referees %</th>
<th>CMP Participants No.</th>
<th>CMP Participants %</th>
<th>Performance Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrosine Crystal</td>
<td>21</td>
<td>95.5</td>
<td>4144</td>
<td>94.3</td>
<td>Good</td>
</tr>
</tbody>
</table>

The arrowed objects are tyrosine crystals. Tyrosine crystals are rare and their presence in urine is always abnormal. They form clusters of silky needle-like structures that are colorless, or black on focusing. Tyrosine crystals are found in acid urine, increase after refrigeration, and are insoluble in alcohol or ether. They are soluble in dilute hydrochloric acid, alkali and relatively heat soluble. An orange color reaction with the nitrosonaphthol test is confirmatory.

Tyrosinuria occurs with liver disease. This may be as a result of a generalized amino acid disorder of liver disease, a transient condition seen in low birth weight or premature infants, or a genetic disorder involving tyrosine metabolism.

The genetic disorders are autosomal recessive. Type 1 hereditary hypertyrosinemia involves defects in fumarylacetoacetate hydrolase and maleylacetoacetate hydrolase. This results in liver failure, renal dysfunction, rickets, and acute intermittent porphyria-like symptoms.

Type 2 is due to deficiency of tyrosine aminotransferase. Patients have erosions of the corneas, soles and palms and variable mental retardation.

Type 3 is very rare and is due to a deficiency of 4-hydroxyphenylpyruvate dioxygenase. Tyrosine levels are less elevated than in the other types. Tyrosine crystals are usually not seen in the urine. The patients have ataxia, seizures and mild psychomotor retardation.
Urine Sediment Photomicrographs/Photographs

Case History CMP-05

This urine sample is from a 56-year-old male with kidney and liver failure. Laboratory data include: Specific gravity 1.012, pH = 5, blood, protein, and leukocyte esterase = positive; glucose, ketones, nitrite = negative. Crystals were soluble in HCl.

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</thead>
<tbody>
<tr>
<td>Cellular Cast</td>
<td>18</td>
<td>100.0</td>
<td>4340</td>
<td>98.7</td>
<td>Good</td>
</tr>
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</table>

The arrowed object is a cellular cast. Cellular casts are composed of a matrix and cellular elements. Casts are increased in kidney disease. Cast formation increases with stasis, increased protein excretion and lower pH. When possible, the main cell type seen in the cast matrix should be specified. If that is not possible, the term “cellular cast” is appropriate.

Red cell casts are identified by the presence of recognizable erythrocytes within the matrix. Red cell casts indicate bleeding within the kidney (e.g. glomerulonephritis).

Some casts are composed primarily of white cells. Still others include renal tubular cells or a mixture of cells and possibly bacteria. White cell and mixed casts indicate kidney inflammation, such as an infection. Renal tubular cells are difficult to specifically identify in cellular casts. The cells have large eccentric nuclei, sparse granular cytoplasm and tend to be elongated or columnar. If they are identified, they indicate renal tubular damage or destruction.

As cellular casts degenerate, they lose identifiable cellular elements and become coarsely and finely granular casts, or in the case of red cell casts, hemoglobin or pigmented casts.
Urine Sediment Photomicrographs/Photographs

Case History CMP-06
This urine sample is from a 56-year-old male with kidney and liver failure. Laboratory data include: Specific gravity 1.012, pH = 5, blood, protein, and leukocyte esterase = positive; glucose, ketones, nitrite = negative. Crystals were soluble in HCl.

<table>
<thead>
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<th>CMP Participants No.</th>
<th>%</th>
<th>Performance Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte</td>
<td>17</td>
<td>100.0</td>
<td>4230</td>
<td>96.1</td>
<td>Good</td>
</tr>
</tbody>
</table>

The arrowed object is a leukocyte. The predominant type of white cell in the urine is the polymorphonuclear neutrophil, or PMN. White cells in the urine are approximately 10-12 microns in diameter, or about twice the size of red cells. The nucleus is lobulated. Normal urine may contain a small number of white cells (0-5 per HPF). The presence of increased numbers of white cells in the urine is termed leukocyturia and is most often seen with urinary tract infection.

Leukocytes should not be confused with urothelial (transitional) cells or renal tubular cells. Urothelial cells line the bladder, ureters and bladder. They are large, measuring 20-30 microns. They are usually spherical with a large round or oval nucleus, often appearing swollen. Renal tubular cells originate in the tubules of the kidney, and have granular cytoplasm. They are about twice the size of a leukocyte, tend to be columnar or elongated, with a round, eccentric nucleus.
Urine Sediment Photomicrographs/Photographs

Case History CMP-07
This urine sample is from a 56-year-old male with kidney and liver failure. Laboratory data include: Specific gravity 1.012, pH = 5, blood, protein, and leukocyte esterase = positive; glucose, ketones, nitrite = negative. Crystals were soluble in HCl.

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<th>Performance Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucus threads</td>
<td>16 100.0</td>
<td>4346 98.7</td>
<td>Good</td>
</tr>
</tbody>
</table>

The arrowed material is mucus. Mucus is a normal finding in urine sediment and tends to form “threads”. It is colorless and can be dissolved by mucolytic agents if it interferes with microscopic examination. Mucus forms long, ribbon-like structures with undefined edges and pointed or frayed ends. They are better seen with low light or phase contrast.

Mucus threads may be confused with hyaline casts, but tend to be irregular, longer and with less defined edges.

Mucus threads are seen more often in specimens from females and often represent vaginal secretions. Proper collection of a clean voided midstream urine reduces this type of contamination.

Roberta Zimmerman, MD
Hematology and Clinical Microscopy Resource Committee
Body Fluid Photomicrographs/Photographs

Case History CMP-08

The patient is a 27-year-old female with relapsed AML, S/P chemotherapy and bone marrow transplant, with total lymphoid irradiation as a preparatory regimen. She presents with symptoms of diplopia. Laboratory findings are as follows: total nucleated cells = 638/μL; RBC = 180/μL.

<table>
<thead>
<tr>
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<th>%</th>
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</thead>
<tbody>
<tr>
<td>Lymphocyte</td>
<td>25</td>
<td>100.0</td>
<td>3049</td>
<td>98.7</td>
<td>Good</td>
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</table>

The arrowed cell is a lymphocyte and was correctly identified by 100% of referees and 98.7% of participants. A lymphocyte is a small, round to ovoid cell which may range in size from 7 to 15 um with usually high but variable nucleus:cytoplasm (N:C) ratios. While most lymphocytes are small with round to oval nuclei, some normal lymphocytes are medium-sized due to an increased amount of cytoplasm which occasionally may be granular. Chromatin is diffusely dense or coarse and clumped. Nucleoli, if present, are small and inconspicuous. As seen in the current arrowed lymphocyte, there is fraying of the cytoplasmic edges which is artifactual. It is important to note the size difference between the arrowed small lymphocyte and the surrounding blast cells.
Body Fluid Photomicrographs/Photographs

Case History CMP-09

The patient is a 27-year-old female with relapsed AML, S/P chemotherapy and bone marrow transplant, with total lymphoid irradiation as a preparatory regimen. She presents with symptoms of diplopia. Laboratory findings are as follows: total nucleated cells = 638/μL; RBC = 180/μL.

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<th>Performance Evaluation</th>
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</thead>
<tbody>
<tr>
<td>Blast cell</td>
<td>24</td>
<td>96.0</td>
<td>2816</td>
<td>91.3</td>
<td>Educational</td>
</tr>
</tbody>
</table>

The arrowed cell is a blast (or myeloblast) and was correctly identified by 96% of referees and 91.3% of participants. Myeloblasts are the most immature cells in the myeloid series. The myeloblast is an intermediate to large cell, 15-20 microns in diameter with a high N:C ratio, round to irregular nuclear membranes, fine or lacy to granular chromatin, distinct nucleolus or multiple nucleoli and basophilic cytoplasm which may exhibit delicate granules or Auer rods.
Body Fluid Photomicrographs/Photographs

Case History CMP-10

The patient is a 27-year-old female with relapsed AML, S/P chemotherapy and bone marrow transplant, with total lymphoid irradiation as a preparatory regimen. She presents with symptoms of diplopia. Laboratory findings are as follows: total nucleated cells = 638/μL; RBC = 180/μL.

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<th>Performance Evaluation</th>
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<tr>
<td>Mitotic Cell</td>
<td>24</td>
<td>96.0</td>
<td>2826</td>
<td>91.6</td>
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The arrowed cell is a mitotic cell and was correctly identified by 96% of referees and 91.6% of participants. Cells undergoing mitoses can be seen in body fluids. Mitotic figures denote actively dividing cells and cells that demonstrate mitotic figures are either reactive cells capable of dividing (lymphocytes, mesothelial cells, synovial cells) or neoplastic cells (leukemia, lymphoma, and carcinoma). Reactive dividing cells demonstrate normal mitotic figures with well aligned chromosomes dividing along a single plate. Neoplastic cells can demonstrate normal or abnormal (multipolar, no evidence of a spindle or irregular distribution of the chromosomes).

Discussion

Acute leukemia blast cells can involve the central nervous system (CNS) at the time of initial diagnosis or at relapse and is known as leukemic meningitis. Blasts may be present in the central nervous system at relapse prior to involvement of the peripheral blood or bone marrow.

It is important to be aware of potential false positive diagnoses of leukemic CNS involvement. One potential and common false positive occurs when there is peripheral blood involvement of the leukemic cells. If blast cells are present in the peripheral blood, a false-positive diagnosis of CNS involvement can occur from contamination of the cerebrospinal fluid (CSF) by peripheral blood during the lumbar puncture procedure. The presence of a lower proportion of blasts in the CSF than in the peripheral blood may indicate contamination, particularly if the CSF is bloody or if the CSF nucleated cell count is low.

A rare instance of false positivity may occur when small numbers of blasts are seen in the CSF as the result of bone marrow contamination (from the vertebrae) during lumbar puncture. Additional findings in this
instance would include other bone marrow cells such as erythroid precursors, myeloid precursors, megakaryocytes and possibly plasma cells.

The current case shows a cellular CSF specimen which consists of a large number of blast cells. Due to the large numbers of blast cells seen in a background of very rare red blood cells this is consistent with leukemic meningitis. Our current patient has been previously treated with chemotherapy as well as bone marrow transplant, thus these findings indicate a relapsed acute myeloid leukemia in the CNS. This finding is also consistent with the clinical findings of focal neurological abnormalities (in this case diplopia) which are common neurological symptoms seen in leukemic meningitis.

It is important to recognize blast cells from other cells which may be seen in the CSF such as lymphocytes and monocytes. As noted in the cell identification, lymphocytes are typically smaller than myeloblasts, have a higher N:C ratio, round and smooth nuclear membranes, contain coarse chromatin and lack a prominent nucleolus. As seen in our current case, the blast cells are intermediate to large in size, contain irregular nuclei and prominent nucleoli. Blasts may be difficult to distinguish from monocytes due to the similar size and irregular nuclear contours. However, monocytes typically have a lower N:C ratio, lack prominent nucleoli and have a lighter basophilic cytoplasm. Also blast cells are highly proliferative and mitotic figures can be commonly seen, a feature not typically seen in normal CSF specimens.

Prompt identification of leukemic involvement of the CNS is important for clinical treatment and resolution of neurological symptoms. With the finding of leukemic meningitis, additional locally directed treatment may be indicated.

It is important to recognize blast cells from other cells which may be seen in the CSF such as lymphocytes and monocytes. As noted in the cell identification, lymphocytes are typically smaller than myeloblasts, have a higher N:C ratio, round and smooth nuclear membranes, contain coarse chromatin and lack a prominent nucleolus. As seen in our current case, the blast cells are intermediate to large in size, contain irregular nuclei and prominent nucleoli. Blasts may be difficult to distinguish from monocytes due to the similar size and irregular nuclear contours. However, monocytes typically have a lower N:C ratio, lack prominent nucleoli and have a lighter basophilic cytoplasm. Also blast cells are highly proliferative and mitotic figures can be commonly seen, a feature not typically seen in normal CSF specimens.

Prompt identification of leukemic involvement of the CNS is important for clinical treatment and resolution of neurological symptoms. With the finding of leukemic meningitis, additional locally directed treatment may be indicated.
References:


Case History CMP-11

The patient is a 93-year-old male with a history of bladder carcinoma admitted to the hospital with complaints of shortness of breath and weakness. A CT scan showed bilateral pleural effusions. A thoracentesis was performed. Laboratory values obtained from the pleural fluid are as follows: RBC = 39690/μL, total nucleated cells = 139/μL, neutrophils = 21%, lymphocytes = 11%, monocytes = 16%, mononuclear cells = 52%, NRBC 4 per 100 WBC. Gross appearance: bloody.

<table>
<thead>
<tr>
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<th>%</th>
<th>Performance Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil segmented or band</td>
<td>23</td>
<td>100.0</td>
<td>2924</td>
<td>97.7</td>
<td>Good</td>
</tr>
</tbody>
</table>

The arrowed cell is a segmented/band neutrophil and was correctly identified by 100% of referees and 97.7% of participants. Segmented neutrophils are 10 to 19 um in size. Segmented neutrophils have condensed, mature nuclear chromatin and segmented or lobated nuclei (2 to 5 lobes typically) which are connected by a thin filament. The characteristic cytoplasm contains numerous fine pink-lilac cytoplasmic granules.
Case History CMP-12

The patient is a 93-year-old male with a history of bladder carcinoma admitted to the hospital with complaints of shortness of breath and weakness. A CT scan showed bilateral pleural effusions. A thoracentesis was performed. Laboratory values obtained from the pleural fluid are as follows: RBC = 39690/μL, total nucleated cells = 139/μL, neutrophils = 21%, lymphocytes = 11%, monocytes = 16%, mononuclear cells = 52%, NRBC 4 per 100 WBC. Gross appearance: bloody.

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<th>%</th>
<th>Performance Evaluation</th>
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</thead>
<tbody>
<tr>
<td>Nucleated red cell</td>
<td>23</td>
<td>100.0</td>
<td>2960</td>
<td>98.9</td>
<td>Good</td>
</tr>
</tbody>
</table>

The arrowed cell is a nucleated red cell and was correctly identified by 100% of referees and 98.9% of participants. Later stage nucleated red blood cells (orthochromatophilic) have dense pyknotic round nuclei and pink cytoplasm. Nucleated red blood cells are uncommonly found in body fluids and may represent peripheral blood contamination. If earlier stage nucleated RBCs (polychromatophilic normoblast, basophilic normoblast, pronormoblast) are present in body fluids and not in the peripheral blood, this may represent accidental aspiration of the bone marrow from either a rib or vertebrae during the fluid collection procedure. Nucleated red blood cells have a homogeneous agranular cytoplasm which distinguishes it from a necrobiotic neutrophil with granular cytoplasm.
Body Fluid Photomicrographs/Photographs

Case History CMP-13

The patient is a 93-year-old male with a history of bladder carcinoma admitted to the hospital with complaints of shortness of breath and weakness. A CT scan showed bilateral pleural effusions. A thoracentesis was performed. Laboratory values obtained from the pleural fluid are as follows: RBC = 39690/μL, total nucleated cells = 139/μL, neutrophils = 21%, lymphocytes = 11%, monocytes = 16%, mononuclear cells = 52%, NRBC 4 per 100 WBC. Gross appearance: bloody.

<table>
<thead>
<tr>
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<th>CMP Participants No.</th>
<th>CMP Participants %</th>
<th>Performance Evaluation</th>
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<tbody>
<tr>
<td>Mesothelial cell</td>
<td>22</td>
<td>95.7</td>
<td>2771</td>
<td>92.9</td>
<td>Educational</td>
</tr>
</tbody>
</table>

The arrowed cell is a mesothelial cell and was correctly identified by 95.7% of referees and 92.9% of participants. Mesothelial cells are large cells (20-50 um) which line the pleural, pericardial and peritoneal cavities and have a low N:C ratio. Mesothelial cells can be seen in increased numbers in fluid samples when associated with inflammatory processes and in malignancies. The nucleus of a mesothelial cells is round to oval in shape with evenly distributed, dense to fine nuclear chromatin and well defined nuclear membranes and one or more nucleoli may be seen. In reactive conditions, multinucleation may be seen. The cytoplasm may appear "two-toned" with an inner or perinuclear lighter basophilic area and a peripheral darker basophilic tone and vacuoles may be present. Mesothelial cells may desquamate singly, in sheets or in clusters and may be mistaken for metastatic malignant cells. However, mesothelial cells when found in clusters have articulated or scalloped cells borders with a discontinuous outer border between cells (clear space or "windows").

Kathryn A. Rizzo, DO, PhD
Hematology and Clinical Microscopy Resource Committee
Discussion

Pleural serous effusions are typically classified under one of two categories, either transudate or exudate. Categorization depends on parameters such as gross appearance of the effusion fluid, total protein ratio, lactate dehydrogenase (LDH) ratio and LDH levels. It is important to categorize the fluid as it has clinical significance since each category is associated with specific etiologies. The gross appearance of the effusion fluid of the current case is bloody, a feature more commonly seen in an exudate. Common causes of an exudative pleural effusion include malignancy, infection, trauma, pulmonary infarction, pulmonary embolism, autoimmune disorders, pancreatitis and ruptured esophagus. Thus for exudative effusions, additional testing such as cytological analysis, fluid culture and gram staining, flow cytometric analysis and diagnostic biopsy may be required for diagnosis.

The current case contains 21% neutrophils as seen in the first cell identification. Although the neutrophil contains cytoplasmic vacuoles, no intracellular microorganisms are identified in the neutrophil or adjacent macrophage. The neutrophils are likely present in the fluid secondary to peripheral blood involvement of the effusion rather than secondary to a bacterial infection.

Pleural fluid typically contains mesothelial cells which are the cells which line the pleura. Although these cells are normally seen, they share similar features with other normal cellular constituents in effusion fluid as well as neoplastic metastatic carcinoma cells. Mesothelial cells may be mistaken for macrophages, a typical fluid constituent. Our final cellular identification shows an arrow pointing to a mesothelial cell which is seen underneath two macrophages engulfing red blood cells. It is common to see macrophages with engulfed red blood cells and/or phagocytic debris, a feature which distinguishes it from mesothelial cells. Macrophages may have oval to elongated nuclei, dense and reticular to coarsely clumped chromatin and typically lack or have indistinct nucleoli. Mesothelial cells typically have round to oval nuclei which tend to be pericentrically placed, distinct nuclear membranes, evenly distributed chromatin and prominent nucleolus. The cytoplasm in macrophages typically contains phagocytized cells and debris versus mesothelial cells which have a biphasic basophilic cytoplasm.

It is clinically significant to distinguish mesothelial cells from metastatic carcinoma cells which involve the effusion fluid. There are a number of morphological differences that distinguish a metastatic malignant cell from a normal benign metastatic carcinoma cell.

Malignant cells often have increased N:C ratios. The nuclear membrane may be indistinct with jagged or projected membranes and the nucleus tends to be irregular. The chromatin pattern tends to have an irregular or uneven coarseness. The nucleolus is typically present and is quite large with irregular borders. Although multinuclearity commonly occurs in benign mesothelial cells as is depicted in our cell identification, when multi-nucleation occurs in a malignant carcinoma cell, the nuclei tend to be haphazardly arranged with marked variation in size, shape and chromatin pattern.

Low power evaluation also shows certain characteristics in a malignant effusion fluid. The malignant cell population appears as a distinct second population versus the population of normal cellular constituents present in the background. The malignant cells can be seen in large spheres with smooth contours as well as single cells which are typically larger than the normal cellular constituents. Mesothelial cells may also cluster; however the cells are typically separated by “windows” and the clusters typically have scalloped or
knobby edges. The clustered mesothelial cells also do not appear as a separate cell population since the morphological features (such as size) are similar to the single mesothelial cells seen in the background.

In our current case, metastatic bladder (urothelial) carcinoma cells are seen to the right of the arrowed mesothelial cell and clustered adjacent to the arrowed neutrophil. Although the metastatic carcinoma cells are similar in size to the mesothelial cell, one can appreciate the cellular differences. The carcinoma cells have a higher N:C ratio, irregular jagged nuclear membranes, irregular nuclei and occasional cells contain distinct irregularly shaped nucleoli.

In men, metastatic genitourinary (kidney, prostate, bladder) carcinoma is a common tumor which causes malignant pleural effusions. In some cases distinguishing malignant involvement versus reactive normal constituents may be difficult to perform on cytological evaluation alone and may require additional ancillary studies (immunohistochemical analysis).

References:


This photograph shows an unstained smear containing fungus and yeast. A 10% KOH (potassium hydroxide) solution is excellent for eliminating background proteinaceous material while leaving the thick chitinous cell walls of the fungi, yeast and arthrospores behind. These elements are clearly outlined for identification.

No eosinophils are identified in this picture. The one cell present is a squamous epithelial cell. Nasal smears for eosinophils are useful for determining the nature of the nasal discharge, with eosinophils associated with allergic rhinitis. Nasal discharge not associated with allergy may be acellular or may show a predominance of neutrophils.
### Pinworm or pinworm eggs are present

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Pinworm or pinworm eggs are present</td>
<td>19</td>
<td>2304</td>
<td>98.5</td>
</tr>
</tbody>
</table>

This unstained preparation demonstrates an *Enterobius vermicularis* egg which is known as pinworm. Humans are considered to be the only hosts of *Enterobius vermicularis*. Transmission occurs by transferring infected eggs to the mouth with hands that scratch the perianal region. Person to person transmission can occur through handling of infected bed linens or clothes. Treatment consists of mebendazole and albendazole.
Ferning is present in this vaginal smear. The fern test is used to detect ruptured amnionic membranes and the early onset of labor. Sometimes the fern test is used to differentiate amniotic fluid from urine. The accuracy of this test is reported to be 84-100%. False positive test can come from cervical mucus. The nitrazine test is also often performed to test the generally neutral pH of the amniotic fluid, whereas the vaginal fluid is usually acidic.

Neutrophils are present among the bacteria on this stool specimen. Assessment of stool specimens for neutrophils is a test that can be used in conjunction with bacterial culture in the evaluation of enteritis/colitis. Though neutrophils are consistent with a bacterial infection, this finding is not specific. Stool cultures are more sensitive and specific for evaluation of enteric pathogens.
This photomicrograph demonstrates an unstained vaginal wet preparation containing sperm. The wet preparation may be examined to diagnose cause of vaginal discharge or to determine the presence of sperm in a case of rape investigation. A sample of vaginal secretion is taken from the posterior vaginal pool using a cotton or dacron tipped swab and mixed with saline on a slide. The sperm head is about 4-6 micrometers in length while the slender tail is about 40-60 micrometers in length.